UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,892	11/26/2007	Antti Haapalinna	06267.0132	4440

22852 7590 09/13/2011

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
RAO, SAVITHA M	

ART UNIT	PAPER NUMBER
1629	

MAIL DATE	DELIVERY MODE
09/13/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,892	HAAPALINNA ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1629	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,2 and 8* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-2 and 8* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending

Receipt and consideration of Applicants' amended claim set and remarks/arguments filed on 06/30/2011 is acknowledged. Claim 1 is amended. Claims 3-6 remain withdrawn from consideration as being drawn towards nonelected specie. Claims 1-2 and 8 are under consideration.

Applicants' arguments, filed 06/30/2011, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Rejection of claims 1-2 and 8 under 35 U.S.C. 103(a) as being unpatentable over Puurunen et al (Neuropharmacology 40 (2001) 597-606) in view of Ginsberg et al (Stroke, 1989; 20, pages 1627-1642) as evidenced by Leker et al (Brain Research Reviews, 42, 2003, pages 187-203) (all the references already of record) is maintained for reasons of record restated below.

Puurunen et al. discloses that systemic administration of atipamezole facilitates recovery following transient focal cerebral ischemia in rats (abstract) Puurunen et al. discloses that atipamezole rapidly penetrates the brain and increases the release of central noradrenaline. Puurunen et al. Also discloses that atipamezole is a potent alpha2-adrenoceptor antagonist with a high alpha2/alpha1 selectivity ratio with negligible affinity for other receptors such as 5-HT and imidazoline receptors (page 598, left col., 2nd paragraph). Puurunen et al. discloses brain ischemic induction in rats and treatment of these rats with atipamezole hydrochloride in sterile water administered

once a day (1 mg/kg subcutaneously), beginning on day 2 of the ischemic induction and continuing for 10 days (page .598, methods, sections 2.1 and 2.2). Puurunen et al. discloses that atipamezole is well –tolerated over a wide range of doses and that atipamezole improved behavioral performance of ischemic rats and accordingly provides a promising pharmaceutical approach to facilitate the recovery process following cerebral ischemia (page 604, right col., last paragraph).

With respect to instant claim 8, Puurunen teaches the use of Atipamezole hydrochloride in his method and as such renders this claim obvious.

Puurunen does not teach the administration of the drug to human patient at risk of developing epilepsy.

However, animal testing in biomedical research is used as a reflection of the final outcome in humans. As disclosed by Ginsberg et al the use of physiologically regulated, reproducible animal models is crucial to the study of ischemic brain injury-both the mechanisms governing its occurrence and potential therapeutic strategies (abstract), Ginsberg additionally teaches that rodent species are readily available at low cost and are widely employed for this purpose (abstract). In addition Ginsberg teaches that Rodents have close resemblance of the cerebrovascular anatomy an physiology to that of higher species (page 1627, right col., 1st paragraph). Accordingly, it would have been obvious to an ordinarily skilled artisan to extrapolate the results obtained by Puurunen et al which clearly recites the beneficial effects of atipamezole as a promising pharmaceutical approach to facilitate the recovery process following cerebral ischemia. in rats to that of mammals and specifically humans and as such develop a method of

treating human patients with brain ischemia with atipamezole. An ordinarily skilled artisan will be imbued with at least a reasonable expectation of success that such a method would provide an alternative and potentially better therapeutic treatment procedure for brain ischemia.

Leker et al is used here as evidentiary document to demonstrate that cerebral ischemia leads to epileptic attack. Leker et al teaches that epileptic seizures may be the result of cerebral ischemia and may also cause brain damage and additionally, suggests that the pathological mechanisms leading to epileptic seizures are identical to those involved in cerebral ischemia (page 188, left column). Leker additionally teaches that experimental models using focal ischemia, usually obtained by occlusion of the middle cerebral artery are representative of stroke pathophysiology (page 190, right col. Last paragraph to page 191, left col. 1st paragraph). As such an ischemic patient would essentially be at risk of epileptic seizures. Therefore, when a patient with brain ischemia is treated with atipamezole, the compound will inherently inhibit the development of epilepsy upon administration. As such, the active step including the subject are in the method of Puurunen et al. i.e., the method of administration of atipamezole to a patient who is at risk of developing epilepsy, is the same as that which is instantly claimed and the method of inhibiting the development of epilepsy in such a subject will thereby be inherent to atipamezole used in the method of Puurunen. It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In

such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph. It is also noted that "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). As such the instantly claimed mechanistic functions of the compounds to inhibit the development of epilepsy would be present in the identical compound being administered to human suffering from brain ischemia as taught by Puurunen et al. and Ginsberg et al. and would therefore elicit these effects whenever it is administered.

Response to applicant's arguments filed on 06/30/2011

Applicants traverse the above rejection with the following arguments.

a. Puurunen alone, or in combination with Ginsberg and Lekar fails to teach or disclose a method for inhibiting the development of epilepsy in accordance with the pending claims.

b. Ginsberg does not mention administering selective α2-adrenoreceptor antagonists to human patient at risk of developing epilepsy.

c. Lekar fails to include any discussion on anti-epileptic effect of α2-adrenoreceptor antagonists. Lekar's results are inconclusive and are unlikely to lead one of ordinary skill in the direction of the claimed methods since Lekar teach that global ischemia

animal model should not be taken as proof of neuroprotective capabilities relevant to stroke and as such teaches away from the instant claims.

d. Puurunen also discloses that atipamezole's disclose effect in rats may not be same in human patients, and as such extrapolating result from rat models to humans in studying cerebral ischemia is rather unpredictable.

e. Atipamezole has been reported to potentiate kainic acid induced convulsion and mortality in rats as such it is unclear as to how office arrived that one of ordinary skill in the art would have expected α2-adrenoreceptor antagonists such as atipamezole to "inherently inhibit the development of epilepsy upon administration of atipamezole.

Applicants arguments are considered but is found to be unpersuasive.

First, it should be noted that the above rejection was made under 35 U.S.C. 103(a) and therefore none of the cited references has to teach every limitation of the instant claims. Applicant is further reminded that the obviousness rejection is not an anticipation rejection. In obviousness rejection a combination of references is used, and the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references that make up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the combination of the cited references. *In re Young*, 403 F.2d 754, 159 USPQ 725(CCPA 1968); *In re Keller 642 F.2d 413, 208 USPQ 871 (CCPA 1981).* Moreover, it is noted that rejections under 35 U.S.C. 103(a) are based on combinations of references, where the secondary references are cited to reconcile the deficiencies of

the primary reference with the knowledge generally available to one ordinary skill in the art to show that the differences between Applicant's invention and the prior art are such that they would have been modifications that were *prima facie* obvious to the skilled artisan. It is noted that the claimed invention is not required to be expressly suggested in its entirety by any one or all of the references cited under 35 U.S.C. 103(a). Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981.)

In the instant case, the references recited in the rejection above renders the instant invention obvious to an ordinarily skilled artisan since Puurunen teaches that systemic administration of atipamezole facilitates recovery form transient focal cerbral ischemia in rats and discloses treatment of rats with brain ischemia with atipamezole hydrochloride. Ginsberg et al. teaches the advantages of animal studies in ischemic brain injury and that that rodents have a close resemblance of the cerebrovascular anatomy and physiology to that of higher species and as such a skilled artisan would be motivated to develop a method of treating humans with cerebral ischemia with atipamezole. Laker here is used as evidentiary documents for their teaching that cerebral ischemia leads to epileptic attack. and accordingly an ischemic patient would essentially be at risk of epileptic seizure. Therefore treatment of a patient with cerebral ischemia with atipamezole would inherently reduce their risk of developing epilepsy.

In response to applicant's arguments against each reference individually, one cannot

show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Ginsberg et al. specifically teaches the advantages of animal studies specifically as it relates to cerebral ischemic and it is generally accepted that animal testing in biomedical research is used as the reflection of the final outcome in human. The process of clinical testing and drug development renders the extrapolation from animal testing to humans obvious. Applicants fail to provide any further support in their disclosure that this may not be the case. It is noted that the experimental data in the specification are all generated in animals and the applicants are claiming treatment of human patients.

Lekar is used here as evidentiary document for their teaching that cerebral ischemia leads to epileptic seizures. As such an ischemic patient would essentially be at risk of epileptic seizure. Puurunen et al. discloses the active step and the subject population as instantly claimed which is the administration of atipamezole to the patients at risk of developing epilepsy which are patients with ischemia and Ginsberg teaches the obviousness of extrapolating animal studies to human studies. Lekar et al provides supportive evidence that cerebral ischemic patients are at risk of developing epilepsy. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

In response to applicant's argument that since Lekar teach that global ischemia animal model should not be taken as proof of neuroprotective capabilities relevant to stroke and as such teaches away from the instant claims. Examiner finds this unpersuasive since Lekar specifically discloses that cerebral ischemia puts an individual at risk for epilepsy. It is noted that a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). Furthermore, "[t]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). Applicants argument with regards to Lekar's teaching of focal vs. global ischemia is a features upon which applicant relies which is not recited in the rejected claim(s). It is noted that applicant recites brain ischemia and does not specify if it is focal or global. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). It is noted that once an examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference. In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the

burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph.

Accordingly, the arguments set forth by the applicant are unpersuasive and the rejection is maintained.

Conclusion

Claims 1, 2 and 8 are rejected. No claims are allowed

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally

be reached on Mon-Fri 7.00 am to 4.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Lundgren can be reached at 571-272-5541. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAVITHA RAO/

Examiner, Art Unit 1629

/Jeffrey S. Lundgren/

Supervisory Patent Examiner, Art Unit 1629